

Remarks

After amendment, claims 1-20 remain pending in the present application. Claims 12-13 have been amended to address the Examiner's objection to those claims. No substantive amendment to the claims has been made to place the application in condition for allowance. No amendment has been made to distinguish over the art of record. Support for the amendment to the claims may be found throughout the originally filed application and claims. No new matter has been added by way of this amendment.

The Examiner has objected to or rejected originally filed claims 1-20 under 35 U.S.C. §112, first paragraph and second paragraph, §102(b) and §103. For the reasons which are set forth in detail herein, it is respectfully submitted that the original specification as filed supports the amendment previously made to claim 1, and the cited reference(s) do not anticipate the present invention nor do they render the present invention unpatentable as being obvious over the cited references. It is respectfully submitted that the claims are now in condition for allowance.

The Objection to Claims 12 and 13

The Examiner has objected to claims 12 and 13 for the reasons which are stated in the office action on page 3. In order to address this objection, Applicants have amended claims 12 and 13 to be dependent on claim 11. It is respectfully submitted that claims 12 and 13 are now in proper form.

The §112, First Paragraph Rejection

The Examiner rejected claims 1-20 under 35 U.S.C. §112, first paragraph for the reasons which are stated in the office action on pages 3-4. In essence, the Examiner contends that previously presented claim 1 contains new matter. In response, Applicants direct the attention of the Examiner to the second full paragraph on page 14 which states, in relevant part "*The amount of metal nitrite in the nitrous acid composition may be generally from about 0.01% to about*

1%... by weight.” Given that clear support for the claims, Applicants respectfully request the Examiner withdraw this rejection.

The §112, Second Paragraph Rejection

The Examiner has rejected claims 1-20 under 35 U.S.C. §112, second paragraph for the reasons which are set forth in the office action at the top of page 5. In particular, the Examiner contends that the term “stabilized” is not clearly defined in the specification and it is not clear how and in what way the composition is stabilized. Applicants respectfully traverse the Examiner’s rejection.

Contrary to the Examiner’s contention, there is actually significant support for the use of the term stabilized, in both the context and language of the originally filed application. For example, consider the context of the language on page 4 of our filing (see, first line) “.the pH of the composition either remains relatively constant or decreases...” (emphasis added) because (as per page 7) “...the amount of nitrite ion in the form of nitrous acid is greater than about 35% but no more than about 95% by weight of the total nitrite ion in the solution.” This is a *sine quo non* for the solution to be able to provide disinfection capability over an extended period. Without such stabilization of the nitrite ion as nitrous acid in that range, the pH of the composition would either rise out of an effective stable germicidal range (see, for example, page 9, where the pH of a 30% nitrous acid/nitrite ratio solution rose from 3.75 to 3.92), or if the composition is too acidic (i.e., >95%, see Table 1, page 8) then too much of the HNO₂ would form and rapidly degrade (through the reaction which is shown on the top of page 9) to NO and NO₃⁻, and lose the capacity for extended germicidal activity as the HNO₂ is rapidly depleted.

It is clearly stated, (page 8, under the Table) that “(a)queous solutions of nitrous acid are generally regarded to be unstable” (emphasis added) which decompose by the reactions shown, but despite that general recognition, we have discovered (page 10), “..it is feasible to adjust the concentrations of nitrite in a preferred composition of this invention such that the solution is **stabilized** or slowly reduces in pH value over a prolonged period of time, and is capable of being stored as a pre-mixed one-part composition.” Further, “..the pH values of nitrous acid solutions

which become lower over time.(and).. apparently level off over time when the total metal nitrite concentrations.... are below about 1.0%” This language clearly supports the language in claim 1 wherein “.. the pH of the composition is stabilized at an initial value of around 3.75 or lower, or decreases...to a value as low as around 2.5..”

With further reference to the stabilization of the compositions as taught by the present invention, is the sentence (on page 10, fifth line from the bottom, with reference to the unexpected stability of increasingly acidic nitrous acid compositions) “This surprising finding is inconsistent with past teachings, which stress the increasing instability [emphasis added] of nitrous acid solutions with increasing relative amounts in solution (*i.e.*, at more and more acidic concentrations).”

Given the clear teachings in the specification of the present application as set forth above, it is respectfully submitted that Applicants claims particularly point out and distinctly claim the subject matter which Applicants regard as their invention. It is respectfully submitted that claims 1-20 are in compliance with the requirements of 35 U.S.C. §112.

The Rejection of Claims 1-20 Under 35 U.S.C. §102(b)

The Examiner has rejected claims 1-20 as being anticipated by the disclosure of Benjamin, et al., US Patent Application Publication US2002/0136750 (“Benjamin, et al.”) for the reasons which are set forth in the office action on pages 5-9. For the reasons which are set forth hereinbelow, Applicants respectfully submit that the present invention is not anticipated by the disclosure of Benjamin, et al. for the simple reason that the reference does not disclose *all* of the claimed elements of the present claimed invention, which is required to make out a cogent rejection based upon anticipation.

It is respectfully submitted that there is a very clear distinction between the present invention and the teachings of Benjamin, et al., that the Examiner is overlooking. In particular, the Examiner’s rejection is summarized in the last sentence at the bottom of page 8. In particular, the Examiner argues: “As discussed above, under the principles of inherency, it is

immaterial whether Benjamin recognized that the mixed composition is capable of long term use.” But the Benjamin compositions do not anticipate our discovery, as we describe it. In fact, Benjamin’s compositions do not provide a specific teaching of a concentration of the nitrite component, other than saying (in claim 1) that it should contain a source of nitrite ions, which is later described in their dependent claim 12 as “..the alkali metal nitrite... constitutes 0.5% to 30% by weight of the total dosage form.” Further, Benjamin simply defines the pH of his system as “sufficient to reduce the pH at an environment of use to below pH4,..”.

Those aspects of Benjamin, et al. represent major differences from the present invention, which specifically narrows the level of metal nitrite (not alkali metal nitrite) to require a definite concentration well within Benjamin’s later defined 30%, as an upper range, and below the minimum 0.5%. It is quite apparent, from the context of Applicants’ teaching, that a system that is outside of the defined range may not be efficacious germicidally. That is, the composition must be such that the amount of nitrite ion in nitrous acid form has to fall within the range of 35% and 95%, or else it ***will not function*** as a long term germicide. There are many Benjamin compositions which fall outside of that range, either below or above their general description and requirements.

At least one aspect of the Examiner’s argument is related to the *apparent* similarity between the Benjamin, et al. “below pH 4” and “around 3.75 or lower” of the present invention. The attention of the Examiner is directed to Table 1 (page 8) in the specification, which provides the Percentage of Nitrite as Nitrous Acid at Varying pH values. Below, we have presented a figure for the break point of pH 3.75 to show that a major difference exists (and also figures showing the 35% to 95% range boundaries).

Table 1 (augmented)

Percentage of Nitrite as Nitrous Acid at Varying pH Values		
pH	Nitrous Acid %	Nitrite %
1.5	98.4	1.6

Percentage of Nitrite as Nitrous Acid at Varying pH Values		
→*2.0	95.2	4.8
2.3	90.9	9.1
2.6	83.3	16.7
2.8	76.0	24.0
3.0	66.7	33.3
3.3	50.0	50.0
3.5	38.8	61.2
→*3.6	35.0	65.0
3.75	24.9	75.1
4.0	16.6	83.4
4.5	6.0	94.0
5.0	2.0	98.0

→* boundary pH values corresponding to the defined NO₂⁻/HNO₂ ratios

The difference between requiring at least about 25% [~one-quarter, at pH 3.75] of the nitrite as nitrous acid, in the present invention (or ~ one-third, at the 35% boundary), and the general requirement of 16.6% [one-sixth], as taught in Benjamin (pH 4.0), may seem as if this is less than a major difference to the Examiner. However, the attention of the Examiner is directed to the present teachings on page 9 of the present application, regarding the critical pHs defining solution stability over a 30-day period (as shown below). Note that below a pH of about 3.7 - 3.6, according to the table, the solution pHs will remain relatively stable, or slowly decrease. Above about 3.7, the pH will rise, and the germicidal efficacy of the aged solution will diminish, with decreasing fraction of nitrous acid present. They will not be, as the present invention is entitled, "Long-Acting Disinfecting Nitrous Acid Compositions."

<u>pH at T=0</u>	<u>pH at T=30 days</u>
2.94	2.30
3.12	2.50
3.35	3.25
3.54	3.15
3.75	3.92
3.90	4.35

Note that even at pH 3.90, a 1.0% solution of alkali metal nitrite would not have the inherent, long-term stability as our solution. And neither would a 2%, or a 5%, or a 10%, 20% or even 30% solution. But because the emphasis in Benjamin, et al. is on short-term, mix and use, disinfection, through the immediate generation of Nitrogen Oxide (plus other subsequent NOxides), long-term stability is simply irrelevant to the Benjamin, et al. compositions.

It is respectfully submitted that the Examiner has not made out a cogent case that the present invention is anticipated by the disclosure of Benjamin, et al.

The Rejection of Claims 10-13 15 and 16-19 Under 35 U.S.C. §103

The Examiner has rejected originally filed claims 1-20 as being unpatentable over Xu, et al., in view of Kross, et al., and further in view of Benjamin, et al. for the reasons which are set forth in the office action on pages 9-12. Essentially it is the Examiner's position that the disclosure of Xu, et al., can be combined with the teachings of Kross, et al., further in view of Benjamin, et al. to provide the present invention. Applicants respectfully traverse the Examiner's rejection.

The stark differences between the presently claimed compositions and the compositions which are disclosed by Xu, et al. have been discussed in great detail in a previous submission. In short, Xu, et al., do not disclose compositions which are even remotely related to the present invention, in that the concentration of nitrite and nitrous acid of Xu, et al. is significantly different than in the present invention and the ratio of nitrous acid to total nitrite in the composition falls within specific percentages, which are markedly distinguishable over the compositions of Xu, et al. which are prepared to mimic compositions in the gastrointestinal tract.

There is absolutely no disclosure in Xu, et al. of the present compositions, or the requirement for certain concentrations of a nitrite salt or a relative percentage of nitrous acid to total nitrite salt in the composition which provides a stable composition that exhibits substantial germicidal activity over long periods of time. There is absolutely no suggestion in Xu, et al. of the present invention and there is simply no motivation taught to provide or pursue the instant compositions. The present invention is clearly non-obvious over Xu, et al.

Further to Applicants' arguments made hereinabove, Applicants have additional reasons for the non-obviousness of the present invention. In this regard, Applicants further point out, with respect to the term "stability", as has been defined in great detail hereinabove, the Examiner's objection (see page 10, lines 6-8), with regard to the description that the Xu, et al. compositions evoke stability, in stating that "Even though Xu *et al.* does not report the long term variability of the nitrite solution, it is expected to remain stable because citrate-phosphate is a strong buffer in acidic conditions" (emphasis added). Applicants strongly disagree. The Examiner cites this as analogous to our recitation that "the pH of the composition either remains relatively constant at an initial value of around 3.75 or lower at the time of formulation to a value as low as around 2.5 over a period of at least about two days." It is respectfully submitted that the Examiner has failed to appreciate the major difference in these two situations. As we have previously argued in our last filing [on page 6, 2nd full paragraph, line 8], and which is referenced here "In point of fact, the Examiner's reference to citrate-phosphate buffers remaining pH-stable is inconsistent with ...the changing and decreasing pH values of the inventive compositions.." **Indeed, the very nature of buffers, specifically acid buffers as taught by the cited prior art, is to maintain the pH of a system as to resist *alkaline* or pH raising factors, which may otherwise drive the pH higher in the direction of neutrality.....Ultimately, as ... the buffering capacity is consumed, the pH of the system will rise rather than lower as is the case of the presently claimed compositions."** This is the exact opposite of the present invention and in this manner actually *teaches away*. Moreover, as the Examiner points out, "The buffer solution of Xu *et al.* is considered an "application medium." (See the last line of page 10 of the office action). As pointed out, the compositions of the present invention are *not* buffer solutions, which are used to counter the influence of basic materials introduced to the solution while depleting its own acidity, but solutions where the pH of the

system will tend toward an increasing acidity, as the nitrous acid disproportionates to form, *inter alia*, nitric acid.

The reason why the pH of the inventive compositions will *lower* as claimed can be directly traced to the reaction shown on page 9 of the present application, whereby the degradation of three nitrous acid molecules [3HNO_2], through a change of the +3 valence of the N atom, leads to the creation of a solution of nitric acid [$(\text{H}^+) + (\text{NO}_3^-)$]; where the complete ionization of the resulting nitric acid leads to a more-acidic solution than that of the fractionally ionized HNO_2 progenitive species. Again, acid buffer solutions, such as citric-phosphoric compositions, will invariably rise in pH, upon depletion of the H^+ ion, whereas the inventive compositions will decrease in pH by producing H^+ ions. In our case, a chemical reaction, with electronic changes, is the basis for the pH lowering. In acid buffer solutions, it is simply a changing balance between the anion and its corresponding acid form that is responsible for the buffering effect.

With respect to the teachings of Xu, et al., the Examiner points out that “the levels of metal nitrite disclosed in Xu *et al.* is 0.00050%- 0.0050%” and he interprets the upper range of “about” 0.0050% to be included in the “about 0.01 to 1.0 range claimed herein.” [See last line, of first paragraph]. It is respectfully submitted that the Examiner has made an error here. In point of fact, Xu *et al.* did not indicate a range of 0.00050% - 0.0050% metal nitrite in their publication. Rather, Xu, et al. cited nitrite concentrations [not metal nitrite] of 0.00033% to 0.0033%. The figures cited by the Examiner are those found on page 12 of our previous filed response of December 22, 2006 where, for the purpose of comparison with the Benjamin levels and Applicants’ levels, both expressed as “metal nitrite”, it was presented what the Xu levels would be, if (hypothetically) similarly expressed as metal nitrite. The term metal nitrite never appears in the Xu paper, nor does Xu indicate what form of nitrite was used in their experiments. Xu, et al., simply mention the addition of “nitrite” at different levels to their media. Consequently, it is respectfully submitted that the Examiner’s arguments are further vitiated, when attempts are made to interpret the upper level of Xu’s 0.00033% to 0.0033% nitrite as being included in the present invention’s lower specified metal nitrite concentration of 0.01% in the 0.01% to 1.0% range. Moreover, the Examiner further admits [2nd paragraph, page 11] that

“Xu *et al.* does not expressly disclose the use of metal nitrite to generate nitrous acid...” in connection with a method of disinfection...”over a period of several months.” Consequently, it is Applicants’ position that the Examiner’s two objections, based on Xu *et al.* come down to 1)- a comparison with known buffers (as described hereinabove), which does not apply in the present instance for the reasons cited, and 2)- an overlap of the two ranges 0.00033% to 0.0033%, as nitrite, and 0.01% to 1.0% as metal nitrite, which point in fact, does not exist. It is respectfully submitted that Xu, et al. clearly does not render the present invention obvious.

Turning to Kross, et al, this reference, is perhaps inapposite to the present invention, inasmuch as it teaches certain chlorous acid/chlorite systems for disinfecting meat carcasses. There is absolutely no disclosure in Kross, et al. of a nitrous acid/nitrite system and there is absolutely no suggestion of the present compositions which are based upon nitrous acid/nitrite. Given that Xu, et al. clearly fail to motivate the present compositions, and Kross, et al. are not even related to the same chemical system as in the present invention, it cannot be cogently asserted that the presently claimed compositions are obvious over the disclosure of Xu, et al., in view of Kross, et al. The argument that the Examiner makes that one could take the teachings of Xu, et al., regarding compositions which do not teach the limitations of the present invention or desirability of the chemical characteristics of the present invention and somehow combine that disclosure with Kross, et al., which is directed to a *different chemical system* than the present invention, to produce the presently claimed invention is simply not a cogent argument and should be withdrawn. It is respectfully submitted that the presently claimed invention is clearly non-obvious over the teachings of Xu, et al., in view of Kross, et al.

Benjamin, et al. do nothing to obviate the deficiencies of the Examiner’s rejection. As discussed hereinabove, Benjamin, et al. completely failed to appreciate the compositions according to the present invention given the absence of even an oblique reference or teaching directed to stability, given the immediate use of the compositions in Benjamin, et al.

From another perspective, the present inventors have established that the compositions of the present invention are capable of long-term disinfection, long after any nitrogen oxides have dissipated, which is completely contrary to the Benjamin teachings. The Benjamin, et al.

compositions, with their nitrogen oxides included, are not the same as those of the present invention, where nitrogen oxides may or may not be present. In a 2-year stored composition of the present invention, that showed activity equal to what was found at T=0, there was no remaining gaseous NOxides. The present inventors achieve that stabilization with metal nitrite compositions within the 0.01-1.0% range- there is absolutely no evidence that the full range of the Benjamin alkali metal compositions [*i.e.*, 0.5% - 30%] would be capable of maintaining germicidal capability, particularly those which fall outside of our stipulated range of HNO₃/NO₂⁻ ratios. Below an initial pH of ~2.0, (95% nitrite ion as nitrous acid), there might be so much NO blown off, that long term stability would not be achievable, and these compositions are included in the Benjamin teachings. Similarly above a pH of about 3.6 (35% nitrite ion as nitrous acid), the pH of the solution would drift upwards with time, as we have shown, and pHs from 3.6 to 4.0 are included in the Benjamin teachings. Less acidic nitrite solutions, have *de minimus* activity. Thus, Benjamin, et al. clearly did not appreciate the present invention.

Applicants take issue with the Examiner's comments on page 11, line 4 *et seq.* that "...it is well settled that 'intended use'" prevents the allowability of the claimed invention because "...the prior art discloses the same composition comprising the same composition comprising the same ingredients..." Benjamin *et al.* point out, repeatedly, as Applicants have shown, that the instant composition that is formed immediately upon the combination and application of the mixture, contains nitric oxide and then other nitrogen oxides, as the germicide. That is the "composition" that is basic to Benjamin, as pointed out, in Benjamin, et al. (see paragraph [0027]) where the ingredients "are separately disposed..for admixture at the intended environment to release NO or NO₂ ions." Thus, the operative composition as taught by Benjamin, et al. is the mixture which contains these oxides. In stark contrast, the present invention is directed to compositions with little or none of the originally formed NOxides as the basis for the long-term germicidal efficacy of stabilized or downward drifting pH solutions of the present invention.

Moreover, with respect to the Examiner's argument regarding the teachings by Kross of the use of antimicrobial agents on animal carcasses that "it would be obvious ..to use a metal nitrite in a composition that comprise...well known buffers to make a stabilized composition" in view of the combined teachings of Xu *et al.*, Kross and Benjamin, the point must be made here

that the compositions of the present invention are based on a defined small range of metal nitrite concentrations, within the broad range cited by Benjamin *et al.*, wherein the limited concentrations of nitrite exist in a specifically defined ratio of $\text{HNO}_2/\text{NO}_2^-$ {~0.37 to ~ 19 corresponding to the 35% to 95% nitrite as nitrous acid concentrations}.

As a final note, with respect to the obviousness of the present invention over the cited art, it is respectfully submitted that "conventional wisdom" supports the patentability of the present invention inasmuch as Benjamin, et al. supports the view that because of "conventional wisdom" the compounds disclosed therein must be used very soon after mixing and there is no motivation or suggestion to do otherwise. Indeed, one of ordinary skill, relying on conventional wisdom and the teachings of Benjamin, et al., would *not* do otherwise. In contrast, the genesis of the present invention relies on not following the conventional wisdom and instead, creates an invention which stands in full contrast to the conventional wisdom and the teachings of the art. In fact, Benjamin *et al.* teach that the acid nitrites in the disclosed compositions only work because the NOxides that are generated upon combination quickly *dissipate*, whereas the present invention is directed to compositions where the compositions are active for a much longer time.

It is respectfully submitted that the present invention is non-obvious over the teachings of Xu, et al, in combination with Kross, et al., further in view of Benjamin, et al.

For the above reasons, Applicant respectfully asserts that the claims set forth in the amendment to the application of the present invention are now in compliance with 35 U.S.C. Applicants respectfully submit that the present application is now in condition for allowance and such action is earnestly solicited.

Applicants have not added nor cancelled any claim. No fee is therefore due for the presentation of this amendment. If a determination that any fee is due or any overpayment is made, please charge/credit Deposit Account No. 04-0838. Should the Examiner wish to discuss the present application in an effort to advance its prosecution, the undersigned attorney may be reached at the telephone number set forth hereinbelow.

Respectfully submitted,

COLEMAN SUDOL SAPONE, P.C.

By: 

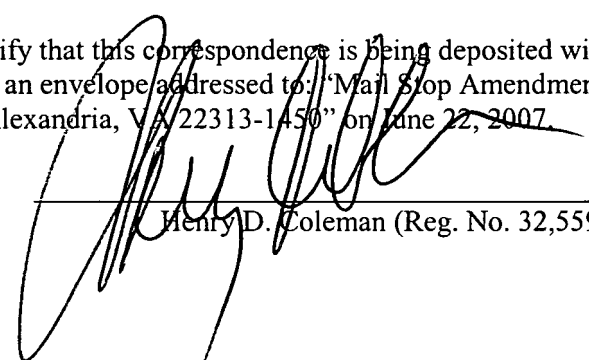
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